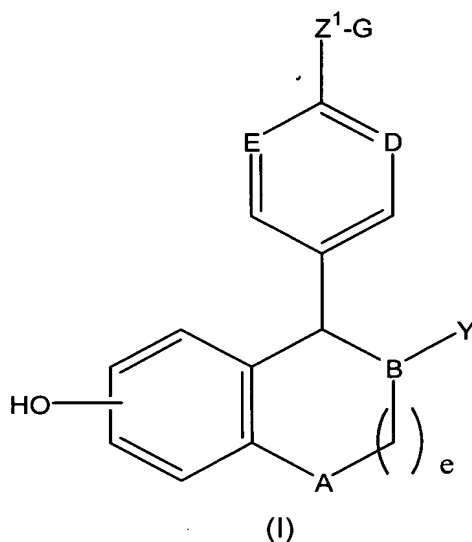


Amendments to the Claims

1. (canceled)

2. (currently amended) ~~The method of claim 4~~ A method of treating benign prostatic hyperplasia in an andropausal male patient, the method comprising administering to an andropausal male patient in need thereof a therapeutically effective amount of an estrogen agonist / antagonist and testosterone, wherein the estrogen agonist / antagonist is a compound of formula I



wherein:

A is selected from CH<sub>2</sub> and NR;

B, D and E are independently selected from CH and N;

Y is

- (a) phenyl, optionally substituted with 1-3 substituents independently selected from R<sup>4</sup>;
- (b) naphthyl, optionally substituted with 1-3 substituents independently selected from R<sup>4</sup>;
- (c) C<sub>3</sub>-C<sub>8</sub> cycloalkyl, optionally substituted with 1-2 substituents independently selected from R<sup>4</sup>;
- (d) C<sub>3</sub>-C<sub>8</sub> cycloalkenyl, optionally substituted with 1-2 substituents independently selected from R<sup>4</sup>;

(e) a five membered heterocycle containing up to two heteroatoms selected from the group consisting of -O-, -NR<sup>2</sup>- and -S(O)<sub>n</sub>-, optionally substituted with 1-3 substituents independently selected from R<sup>4</sup>;

(f) a six membered heterocycle containing up to two heteroatoms selected from the group consisting of -O-, -NR<sup>2</sup>- and -S(O)<sub>n</sub>-, optionally substituted with 1-3 substituents independently selected from R<sup>4</sup>; or

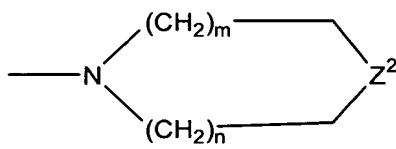
(g) a bicyclic ring system consisting of a five or six membered heterocyclic ring fused to a phenyl ring, said heterocyclic ring containing up to two heteroatoms selected from the group consisting of -O-, -NR<sup>2</sup>- and -S(O)<sub>n</sub>-, optionally substituted with 1-3 substituents independently selected from R<sup>4</sup>;

Z<sup>1</sup> is

- (a) -(CH<sub>2</sub>)<sub>p</sub> W(CH<sub>2</sub>)<sub>q</sub>-;
- (b) -O(CH<sub>2</sub>)<sub>p</sub> CR<sup>5</sup>R<sup>6</sup>-;
- (c) -O(CH<sub>2</sub>)<sub>p</sub>W(CH<sub>2</sub>)<sub>q</sub>-;
- (d) -OCHR<sup>2</sup>CHR<sup>3</sup>-; or
- (e) -SCHR<sup>2</sup>CHR<sup>3</sup>-;

G is

- (a) -NR<sup>7</sup>R<sup>8</sup>;

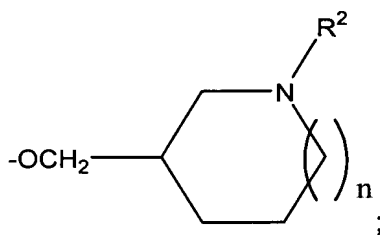


wherein n is 0, 1 or 2; m is 1, 2 or 3; Z<sup>2</sup> is -NH-, -O-, -S-, or -CH<sub>2</sub>-;

optionally fused on adjacent carbon atoms with one or two phenyl rings and, optionally independently substituted on carbon with one to three substituents and, optionally, independently on nitrogen with a chemically suitable substituent selected from R<sup>4</sup>; or

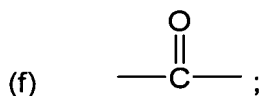
(c) a bicyclic amine containing five to twelve carbon atoms, either bridged or fused and optionally substituted with 1-3 substituents independently selected from R<sup>4</sup>; or

Z<sup>1</sup> and G in combination may be

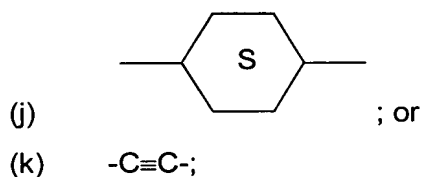


W is

- (a)  $-\text{CH}_2-$ ;
- (b)  $-\text{CH}=\text{CH}-$ ;
- (c)  $-\text{O}-$ ;
- (d)  $-\text{NR}^2-$ ;
- (e)  $-\text{S}(\text{O})_n-$ ;



- (g)  $-\text{CR}^2(\text{OH})-$ ;
- (h)  $-\text{CONR}^2-$ ;
- (i)  $-\text{NR}^2\text{CO}-$ ;



R is hydrogen or  $\text{C}_1$ - $\text{C}_6$  alkyl;

$\text{R}^2$  and  $\text{R}^3$  are independently

- (a) hydrogen; or
- (b)  $\text{C}_1$ - $\text{C}_4$  alkyl;

$\text{R}^4$  is

- (a) hydrogen;
- (b) halogen;
- (c)  $\text{C}_1$ - $\text{C}_6$  alkyl;
- (d)  $\text{C}_1$ - $\text{C}_4$  alkoxy;
- (e)  $\text{C}_1$ - $\text{C}_4$  acyloxy;
- (f)  $\text{C}_1$ - $\text{C}_4$  alkylthio;
- (g)  $\text{C}_1$ - $\text{C}_4$  alkylsulfinyl;
- (h)  $\text{C}_1$ - $\text{C}_4$  alkylsulfonyl;
- (i) hydroxy ( $\text{C}_1$ - $\text{C}_4$ )alkyl;

- (j) aryl (C<sub>1</sub>-C<sub>4</sub>)alkyl;
- (k) -CO<sub>2</sub>H;
- (l) -CN;
- (m) -CONHOR;
- (n) -SO<sub>2</sub>NHR;
- (o) -NH<sub>2</sub>;
- (p) C<sub>1</sub>-C<sub>4</sub> alkylamino;
- (q) C<sub>1</sub>-C<sub>4</sub> dialkylamino;
- (r) -NHSO<sub>2</sub>R;
- (s) -NO<sub>2</sub>;
- (t) -aryl; or
- (u) -OH;

R<sup>5</sup> and R<sup>6</sup> are independently C<sub>1</sub>-C<sub>8</sub> alkyl or together form a C<sub>3</sub>-C<sub>10</sub> carbocyclic ring;

R<sup>7</sup> and R<sup>8</sup> are independently

- (a) phenyl;
- (b) a C<sub>3</sub>-C<sub>10</sub> carbocyclic ring, saturated or unsaturated;
- (c) a C<sub>3</sub>-C<sub>10</sub> heterocyclic ring containing up to two heteroatoms, selected from -O-, -N- and -S-;
- (d) H;
- (e) C<sub>1</sub>-C<sub>6</sub> alkyl; or
- (f) form a 3 to 8 membered nitrogen containing ring with R<sup>5</sup> or R<sup>6</sup>;

R<sup>7</sup> and R<sup>8</sup> in either linear or ring form may optionally be substituted with up to three substituents independently selected from C<sub>1</sub>-C<sub>6</sub> alkyl, halogen, alkoxy, hydroxy and carboxy;

a ring formed by R<sup>7</sup> and R<sup>8</sup> may be optionally fused to a phenyl ring;

e is 0, 1 or 2;

m is 1, 2 or 3;

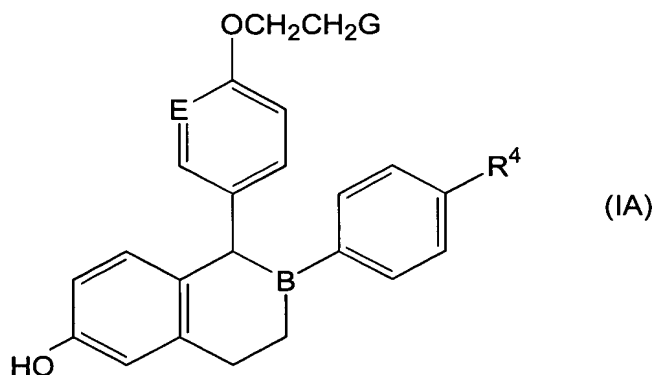
n is 0, 1 or 2;

p is 0, 1, 2 or 3;

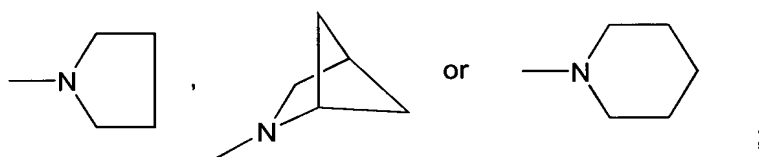
q is 0, 1, 2 or 3;

or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

3. (currently amended) The method of claim 4 2 wherein the estrogen agonist / antagonist is a compound of formula (IA)



wherein G is



R<sup>4</sup> is H, OH, F, or Cl; and B and E are independently selected from CH and N or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or a prodrug thereof.

4. (currently amended) The method of claim 4 2 wherein the estrogen agonist / antagonist is (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol or an optical or geometric isomer thereof; a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or a prodrug thereof.

5. (currently amended) The method of claim 4 wherein the estrogen agonist / antagonist is in the form of a ~~D-tartrate~~ tartrate salt.

Claims 6.-60. (Canceled)

61. (currently amended) A method of treating ~~andropause in a~~ benign prostatic hyperplasia in an andropausal male patient, the method comprising administering to a an andropausal male patient in need thereof a therapeutically effective amount of

(-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol, D-tartrate salt and testosterone.